REMARKS

Claims 30-33 are pending in the application.

Claims 30 to 33 have been rejected under 35 U.S.C. § 101 because the claimed invention allegedly is not supported by a substantial or well-established utility.

Additionally, claims 30-33 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being supported by either a well asserted utility or well established utility.

Applicants respectfully traverse.

Applicants provide herewith a Declaration by Masato Horie dated March 5, 2007. The Declaration herewith supplements and includes corrections to the Declaration dated October 23, 2006. For example, the Declaration supplements the Declaration dated October 23, 2006, in that it explains that the "human NELL1" disclosed in Kang means a polypeptide having an amino acid sequence that is identical with the amino acid sequence of SEQ ID NO:34. The Declaration herewith corrects a typographical in that the correct abbreviation of the "nel-related protein 1" is "NRP1," rather than the incorrect abbreviation of "NPR1."

The Declaration by Masato Horie demonstrates that the claimed nucleic acid molecule is supported by a substantial or well-established utility. Evidence will be sufficient if, considered as whole, it leads a person skilled in the art to conclude that the asserted utility is more likely than not true. *See* MPEP 2107.03 (VII).

In the present case, the Declaration demonstrates the utility of a human NELL-1. The Declaration shows that rat NELL-1 selectively enhances the survival of neuritis and that rat NELL-1 has nerve growth activity. The use of rat NELL-1 is evidence that the claimed nucleic acid molecule has a well asserted or well established utility.

As described in the Declaration, Kang *et al.* "Human *NELL-1* Expressed in Unilateral Coronal Synostosis," Journal of Bone and Mineral Research, vol. 15, no. 1 (1999) pg. 80-89 ("Kang") discloses that the rat NELL-1 has 93 % homology with human NELL-1. In referring to human NELL-1, Kang cites Watanabe *et al.* "Cloning and Characterization of Two Novel Human cDNAs (NELL1 and NELL2) Encoding Proteins with Six EGF-like Repeats," Genomics, 38:273-276 (1996) ("Watanabe"). Watanabe discloses that human NELL-1 comprises the amino acid sequence of SEQ ID NO:34.

In this regard, Applicants respectfully submit that Kang discloses that the rat NELL-1 disclosed in the Declaration has 93 % homology with the nel-related protein type 1 recited in claim 28. The 93 % homology is a sufficiently high level of homology that a person skilled in the art would understand that rat NELL-1 is representative of the nel-related protein type 1 recited in claim 28 for the purpose of establishing the activity of the claimed nel-related protein type 1 recited in claim 28. Similar to the rat NELL-1, a person skilled in the art would understand that the nel-related protein type 1 can also provide for the selective enhancement of the survival of neuritis and the nerve growth activity.

For example, Zhang *et al.*, "Craniosynostosis in transgenic mice overexpressing Nell-1," Journal of Clinical Investigation, vol. 110, no. 6, 861-870 (2002) ("Zhang") discloses in the summary at page 861 that NELL-1 is a molecule expressed during premature cranial suture closure in patients with craniosynostosis. Zhang discloses that Nell-1 DNA-positive transgenic F2 mice, which were created to overexpress rat NELL-1, exhibited craniofacial anomalies and overexpression of Nell-1 RNA in the heads thereof. *See*, page 864, right column, line 38 to left column, line 1. Zhang discloses that the NELL-1 RNA overexpression levels in transgenic mice is clinically relevant to NELL-1 overexpression in human patients with craniosynostosis. *See*,

page 865, left column, lines 3 to 7. Zhang discloses creating an animal model of human nonsyndromic CS by overexpressing rat NELL-1. *See*, page 870, left column, lines 36 to 37. Zhang also discloses that Nell-1 is highly conserved across species. *See*, page 862, left column, lines 37-39. As an example, Zhang discloses that 93 % amino acid sequence homology exists between rat Nell-1 and human NELL-1. In this regard, Zhang demonstrates that a person skilled in the art would recognize that rat NELL-1 is representative of human NELL-1 for the purpose of analyzing the selective enhancement of the survival of neuritis and the nerve growth activity.

As such, the Declaration demonstrates the utility of a human NELL-1. The Declaration shows that rat NELL-1 selectively enhances the survival of neuritis and that rat NELL-1 has nerve growth activity. The use of rat NELL-1 is evidence that the claimed nucleic acid molecule has a well asserted or well established utility.

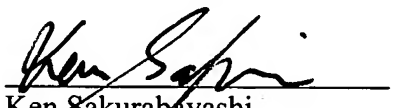
Furthermore, Zhang and Desai *et al.* "*Nell1*-deficient mice have reduced expression of extracellular matrix proteins causing cranial and vertebral defects," Human Molecular Genetics, vol. 15, No. 8 (2006), pp. 1329-1341 ("Desai") are themselves evidence that the claimed nucleic acid possesses utility. Zhang discloses that the infection of osteoblasts with Nell-1 adenoviral constructs showed that Nell-1 promotes and accelerates differentiation in osteoblast lineage cells. *See*, page 862, right column, lines 2-4. Desai discloses that transgenic mice over-expressing rat *Nell1* gene displayed craniosynostosis at birth, thereby confirming the earlier report that Nell1 has a key role in human cranial development and indicating that the underlying mechanisms can be investigated accurately using mouse models. *See* page 1330, left column, lines 26-31. Further, Desai discloses that a NELL1 protein binds to and is phosphorylated by PKC-β1 via the EGF-like domains, indicating that *Nell1* represents a novel class of cell-signal ligand molecules critical for grown and development. *See* page 1330, left column, lines 42-45.

The specification also describes that NRPs might play a brain specific role, for example, as signal molecules for growth regulation. *See* page 90. The specification describes that EGF domain-containing NRPs act a s growth factors in the brain. *See* page 91. The Declaration herewith reproduces and confirms the utility of the claimed DNA sequence and does not add new experimental data.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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